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EXAMINER	
STAPLES, MARK	
ART UNIT	PAPER NUMBER
1637	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,506	SHOEMAKER ET AL.	
	Examiner	Art Unit	
	Mark Staples	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *122,178 and 185-232* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *122,185,189,192,197,200,221-224,226 and 228-232* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/29/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 178,186-188,190,191,193-196,198,199,201-220, 225 and 227.

DETAILED ACTION

1. Applicant's amendment of claims 122 and 178 in the paper filed on 07/29/2008 is acknowledged.

Claims 122, 185, 189, 192, 197, 200, 221-224, 226, and 228-232 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Objections and Rejections that are Withdrawn

Claim Rejections Withdrawn - 35 USC § 103(a)

2. The rejection of claims 122, 185, 189, 192, 197, 200, 221-222, 224, 226, and 228-231 under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (1997, previously cited), Bowtell (1999 previously cited) is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

3. The rejection of claim 223 under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. and Bowtell further in view of Schena et al. is withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection, necessitated by amendment.

New Rejections Necessitated by Amendment

New Claim Rejections - 35 USC § 103

4. Claims 122, 185, 189, 192, 197, 200, 221, 222, 224, 226, and 228-231 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (1997, previously cited), Bowtell (1999 previously cited) and Hui et al. (United States Patent 6,013,436 filed August 19, 1996 and issued January 11, 2000).

Regarding claim 122 and 200, Lockhart et al. teach an array, comprising:
a positionally-addressable ordered array of polynucleotide probes bound to a solid support (entire reference especially Figures 1-4 and column 23 line 28-29: "Probes may be laid out on an polynucleotide array with a specifically defined positional relationship");
and said polynucleotide probes comprising a plurality of at least 100 polynucleotide probes of different nucleotide sequences (entire reference especially Figures 1-4 and claim 1 "at least four hundred different polynucleotides sequences per square centimeter"), each said different nucleotide sequence comprising a sequence complementary and hybridizable to a different genomic sequence of the same species of organism, said different genomic sequences being found at sequential sites in the genome of said species of organism (entire reference, especially Figure 2, Brief Description of the Figures, and SEQ ID NOS: 6-37 for the specie Homo Sapiens), wherein the distance between 5' ends of said sequential sites is always less than 500 bp (entire reference, especially "Single Increment Tiling" found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature

includes nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30 , 25 or 15 nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 300 or less, the distance between 5' ends of any two sequential overlapping sites always must be less than 500 bp; as the maximum 5' distance end to end, which needs to include at least 1 overlapping nucleotide, is 300-1 = 299 bp).

Although this is a new rejection it is noted that Applicant argues that Lockhart et al. only teach probes to polynucleotides/nucleic acid sequences which encode polypeptides and thus argues that probes to introns are not taught by Lockhart et al. However, while Lockhart et al. do specifically teach probes to nucleic acid sequence which encode polypeptides, they do not exclude probes to introns. Furthermore, claim 1 of Lockhart et al. broadly recites probes to polynucleotides and is not limited to polynucleotides/nucleic acid sequences which encode polypeptides (see also the 2nd sentence of the Abstract). Additionally as given above, the teachings of Hui et al. are specifically relied upon for intron probes, and not the teachings of Lockhart et al.

Regarding claim 185, Lockhart et al. teach that a desired level of information may be determined, that is, that one can exclude low information content (see column 12 lines 7-10). As the specification does not provide a closed definition of "low information", this teaching of Lockhart et al. reads on the claim language.

Regarding claim 189, Lockhart et al. an array with probe density ranging from 625 to 10 million probes per 1 cm^2 and thus teach an array having greater than 50,000 different polynucleotide probes per 1 cm^2. (col. 7, lines 1-9).

Regarding claim 192, Lockhart et al. teach an array where the sequences targeted by the probes are spaced apart by less than 200 bp (entire reference, especially "*Single Increment Tiling*" found in column 9 line 62 through column 10 line 7 in which each probe overlaps and where sequence signature include nucleotide sequences at most 300, 250, 200, 150, 100, 75, 50, 30, 25 or 15 nucleotides in length found in column 7 lines 36-38; and thus for overlapping sequences of 200 or less, the distance between 5' ends of any two sequential overlapping sites always must be less than 200 bp; as the maximum 5' distance end to end, which needs to include at least 1 overlapping nucleotide, is 200-1 = 199 bp).

Regarding claim 197, Lockhart et al. teach an array wherein each nucleotide sequence of the array consist of 102-103 nucleotide sequences as given in SEQ ID NOS: 5-37 (See Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claims 221, 222 and 224, Lockhart et al. teach wherein the organism is a human, *Homo Sapiens*, which is a mammal which is an eukaryote (see Sequence Listing for SEQ ID NOS: 5-27 where the organism is *Homo Sapiens*, Figure 5 and 6, Sequence Listing, and description of Figures 5 and 6 found in column 6 lines 49-67).

Regarding claim 226, Lockhart et al. teach an array with at least 10,000 probes by teaching high density arrays, with probe density ranging from 625 to 10 million probes per 1 cm^2. (Fig. 2; col. 6, lines 62-67; col. 7).

Regarding claims 228 and 230, Lockhart et al. teach "The target polynucleotide whose sequence is to be determined can be isolated from a clone, a cDNA, genomic

DNA, RNA, cultured cells, or a tissue sample"; and further teaches "If the target is mRNA, the sample is obtained from a tissue in which the mRNA is expressed" and " sufficient DNA is present in the tissue sample to dispense with the amplification step", in other words the total cellular DNA, which is nucleic acid, is used (see column 21 lines 8-37 and entire reference).

Regarding claim 229, Lockhart et al. teach "The target can be labeled at one or more nucleotides during or after amplification" (see column 21 lines 33-34).

Regarding claim 231, Lockhart et al. teach an array with at least 10,000 different probes by teaching high density arrays of different probes, with probe density ranging from 625 to 10 million probes per 1 cm^2. (Fig. 2; col. 6, lines 62-67; col. 7).

Regarding claim 122, Lockhart et al. do not specifically teach an array wherein the genomic target sequences for a plurality of probes span a genomic region of at least 25,000 bp.

Bowtell teaches microarrays having regions of 42,000 (42k) and 30,000 (30k) gene sets, each of which is over 25,000 bp and that the entire genome of *C. elegans* (entire reference, especially Table 3, 2^{nd} column first two entries, p. 26 column 2 - 2^{nd} paragraph, and supporting document, Human Genome Project, p. 3 chart showing 3 billion base for the human genome and 97 million bases for *C. elgans* genome).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al. by spanning

genomes as suggested by Bowtell with a reasonable expectation of success. The motivation to do so is provided by Bowtell who teach the usefulness of array to span genomes and the teaching of Lockhart et al. that array can span gene families (see Figure 3 and its description in column 5 lines 27-33). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Further regarding claim 122, Lockhart et al. and Bowtell do not specifically teach at least two probes complementary and hybridizable to genomic sequences contained entirely within an intron.

Regarding claim 122, Hui et al. teach intron probes, that is, probes that are complementary and hybridizable to genomic sequences contained within an intron, by teaching intron probes in general and specifically teaching probes/oligonucleotides which are complementary and hybridizable to intron regions of the genomic VHL suppressor gene (see column 3 lines 4-7 and note that the plural "probes" are taught and thus at least two probes are taught) which: " . . . can be immobilized as an array" (see column 10 lines 53 and 54).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrays of Lockhart et al. and Bowtell by including intron probes as suggested by Hui et al. with a reasonable expectation of success. The motivation to do so is provided by Hui et al. who teach intron probes and who teach that intron probes can be used for the diagnosis, specifically diagnosis of the

VHL tumor suppressor gene mutation (see column 3 lines 4-7). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

5. Claim 223 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al., and Bowtell, and Hui et al. as applied to claims 122 and 185 above, and further in view of Schena et al. (1996).

Lockhart et al., and Bowtell, and Hui et al. teach as noted above.

Lockhart et al., and Bowtell, and Hui et al. do not teach wherein the organism is a plant.

Schena et al. teach microarrays to measure expression of plant genes (see 2nd paragraph of p. 10614).

Although this is a new rejection is noted that Applicant argues that Schena et al. only teach probes to cDNA and thus argues that probes to introns are not taught by Schena et al. However, while Schena et al. do specifically teach probes to cDNA, they do not exclude probes to introns. Schena et al. broadly teach the analysis of complete genome sequences by probes which necessarily includes introns (see 1st sentence on p. 10614). Additionally as given above, the teachings of Hui et al. are specifically relied upon for intron probes, and not the teachings of Schena et al.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Lockhart et al., and Bowtell, and Hui et al. by targeting nucleotide sequences of plant genes as suggested by

Schena et al. with a reasonable expectation of success. The motivation to do so is provided by Schena et al. who teach usefulness of microarrays in measuring plant genes and the teaching of Lockhart et al., and Bowtell, and Hui et al. who teach the detection of genes and gene mutations using arrays and microarrays. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Species Election

6. As the claims to elected species remain rejected, the claims to non-elected species are not examined.

Conclusion

7. No claim is free of the prior art.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples
/M. S./
Examiner, Art Unit 1637
October 25, 2008

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637